**ASPERGILLOSIS**

* signs and symptoms:
  + 29 y/o woman w/**dry cough**, SOB, and pleuritic **chest pain** for **more than one week**
    - developed fever, chills, and **bloody cough**
    - **CT= Small pulmonary nodules and a hazy rim (halo sign)**
  + two week prior pt had been admitted for tx of **leukemia**  hospital in the midst of major reconstruction project
  + while hospitalized received **cytotoxic chemotherapy and developed severe neutropenia**
* source of infectious organism: ***Aspergillus fumigatus***
* manner of exposure, route of infection, tissues that they reside and, where appropriate, transmission to others:
  + fungus is ubiquitous in nature and associated w/decaying vegetation
  + inhalation of airborne conidia is major mode of acquisition; not transmitted person to person
* pathology and the manner by which the particular disease develops:
  + invasive pathogen
  + number of adhesins involved in colonization of lower respiratory airways
  + host immune response to the mold determines whether the organisms is cleared or whether disease develops
    - along w/neutrophils, alveolar macrophages are the major cells involved in the phagocytosis of *A. fumigatus*
      * lectin-like interactions are thought to be primarily responsible for the adherence and ingestion of conidia by alveolar macrophages
    - hyphae are destroyed by neutrophils in normal hosts
  + invasive disease develops in pts w/phagocyte deficiencies (chronic granulomatous disease) and primarily in pts w/profound neutropenia
    - in neutropenic pts, *A. fumigates* invades the lungs, producing granulomas that are seen in chest x-rays
  + fungal hydrolases and toxic molecules (e.g. hemolysis) of the angioinvasive pathogen are involved in endothelial damage, causing hemoptysis and other manifestations of invasive pulmonary aspergillosis
* methods of identification and placement into a particular biological subset:
  + classic morphological appearance in stained tissue is that of thin hyphae of even diameter that branch at a V-shaped (45°) angle
  + not dimorphic
  + diagnostic work-up –
    - direct microscopy – acid-fast stain, Gram stain of sputum, cytology staining
    - fungal cultures
    - serum antigen testing for *Aspergillus* galactomannan
    - blood cultures to rule out bacteremia
* factors leading to enhanced resistance or susceptibility
  + **cytotoxic drugs that lead to neutropenia greatly increase susceptibility**
  + an increase in the environmental load of conidia (as may occur during building reconstruction and renovation projects) may lead to increased risk of disease
  + other risk factors include corticosteroid use, organ transplantation, GVHD, and advanced AIDS
  + other organisms in the differential diagnosis and how to discriminate among potential causative agents:
    - differential – aspergillosis, bacterial pneumonia, legionellosis, nocardiosis, pneumocystis pneumonia, zygomycosis
    - rationale – clinical scenario highly characteristic for invasive pulmonary aspergillosis in pts w/neutropenia. While the other organisms listed can also cause severe pneumonia, the CT findings in this case suggest aspergillosis.
* prevention, treatment and vaccine design (live vs. dead):
  + prevention and vaccine – no immunization is available; recovery from neutropenia is necessary, achieved by reducing levels of implicated drugs and administration of colony-stimulating factors such as GCSF
    - high-efficiency particulate air (HEPA) filtration has also been recommended for high-risk patients
  + treatment – amphotericin B standard for therapy for many years, and many amphotericin B lipid preparations are available to help reduce nephrotoxicity
    - voriconazole now considered DOC for invasive pulmonary aspergillosis
    - itraconazole may be considered for use in less immunocompromised pts
    - caspofungin (an echinocandin) considered second-line tx
    - duration in tx depends on improvement in host defenses and severity of diseaes